

### REMARKS

Claims 1-23 and 34-42 are currently pending in the present application. Claims 16-18 are withdrawn from further consideration as being directed to a non-elected species. Claims 1-4, 11, 13, 19, 20, 22-23 and 34-36 have been amended. Claims 37-42 are new. Claims 1-15, 19-23, and 34-36 stand rejected.

Support for the amendment of claims 1 and 11 can be found in the specification at page 29, lines 1-6, page 27, last full paragraph, page 12, first full paragraph and in Figs. 1, 2 and 4. Support for the amendment of claims 1 and 2, new claims 37, 39-41 can be found in the original claims and page 19, lines 14-16. Support for the amendment of claims 13, 19 and 23 can be found in Figures 1 and 2, and page 10, lines 7-26. Support for the amendment of claim 20 can be found at page 7, lines 11-14. Support for the amendment of claims 38 and 42 can be found at page 27, lines 15-18. The amendment of claims 19, 22-23 and 34-36 resolves the antecedent basis deficiencies. No new matter has been added.

Pending claims 1-23 and 34-42 when considered together with the following remarks are believed to be in condition for allowance. Accordingly, early and favorable further action on the merits is earnestly solicited.

### Interview Summary

Applicants note with appreciation that Examiner Lu conducted a personal Interview with Applicants' representative, Mr. Eggerton Campbell, on October 28, 2008. Examiner Lu was very helpful in clarifying the outstanding issues.

During the Interview, the rejection under 35 C.F.R. § 112, second paragraph was thoroughly reviewed and proposed amendments to the claims were looked upon with favor by the Examiner.

Furthermore, the structural differences between the present invention and the closest prior art of Huse *et al* (U.S. 5,378,360) were discussed. In addition, the advantages of an organic polymer having a hydroxyl group on the surface of the solid phase-holding member located only at the first opening part of the apparatus were discussed.

Applicants note that the Examiner Interview Summary form (PTOL-413) resulting from the Interview correctly states the portion of the Interview relating to the cited prior art.

The following paragraph numbers correspond to the numbering of the paragraphs in the Office Action.

**Issues Under 35 U.S.C. § 112, Second Paragraph, Indefiniteness**

4. The Examiner has rejected claims 1-15, 19-23 and 36 under 35 C.F.R. § 112, second paragraph as being indefinite. Reconsideration and withdrawal of the above rejections are respectfully requested based on the following considerations.

With respect to claims 1 and 11, the Examiner alleges that it is unclear if the operation part of a piston member is inside of the syringe or not.

In response to this rejection, claims 1 and 11 have been amended to clarify that the operation part of the pressure difference-generating apparatus extends out of the syringe. Applicants note that the term "operation part" is provided at page 12, first full paragraph and in Figs. 1 and 2 (see element 34).

5. Regarding claim 5, this claim is rejected for allegedly being indefinite for depending upon independent claim 1, which does not require that a solid phase-holding member is a column with a circular shape.

In response to this rejection, amended claim 1 now recites:

*"a solid phase-holding member, comprised of a column with a circular shape".*

6. Regarding claim 13, this claim is rejected for allegedly being indefinite because it is unclear that "an accommodation part" is from the apparatus recited in claim 1 or not.

In response to this rejection, Amended claim 13 now recites:

*"the accommodation part".*

This amendment correlates with the "accommodation part" of claim 1, and clarifies that this is not a new "accommodation part". The word "the" before the recitation of

"accommodation part" establishes antecedent basis back to claim 1.

7. Regarding claims 13 and 20, these claims are rejected for allegedly being indefinite because there is insufficient antecedent basis for the limitation "the pressure change".

In response to this rejection, amended claims 13 and 20 now recite:

*"a pressure change".*

This amendment establishes that the term "pressure change" is a new limitation, not previously recited.

8. Regarding claim 19, this claim is rejected for allegedly being indefinite because it is unclear "a second opening part" is from the apparatus recited in claim 1 or not. Furthermore, it is unclear that "an accommodation part" as recited in claim 19 is from the apparatus recited in claim 1 or not.

In response to this rejection, amended claim 19 now recites:

*"the second opening part into the accommodation part".*

This amendment correlates with the second opening part of claim 1, and clarifies that this is not a new "second opening part". The word "the" before the recitation of "accommodation part" establishes antecedent basis back to claim 1.

9. Regarding claim 20, this claim is rejected for allegedly being indefinite because it is unclear which step in claim 19 is considered as the next step.

In response to this rejection, amended claim 20 now recites:

*"and wherein steps (c) and (e) start after sensing the discharge of sample solution in steps (b) and (d), respectively."*

This amendment clarifies that only in steps (b) and (d), the next step will start after sensing the discharge of sample solution.

10. Regarding claims 23, 35 and 36, these claims are rejected for allegedly being indefinite because there is insufficient antecedent basis for the limitation "the container".

In response to this rejection, amended claims 23, 35 and 36 recite:

*"the accommodation part"*.

This amendment correlates with the "accommodation part" of claim 1, and clarifies that this is not a new "accommodation part". The word "the" before the recitation of "accommodation part" established antecedent basis back to claim 1. Additionally, the accommodation part more accurately describes the area which is able to hold the sample solution.

11. Regarding claim 34, this claim is rejected for allegedly being indefinite because claim 34, which depends upon claim 12, does not establish antecedent basis.

In response to this rejection, amended claim 34 now recites proper antecedent basis for the parts of the claimed apparatus.

12. Regarding claim 36, this claim is rejected for allegedly being indefinite because it is unclear if "a pressure sensor" is from the apparatus recited in claim 1 or not.

In response to this rejection, amended claim 36 now recites:

*"the pressure sensor"*.

This amendment correlates with the pressure sensor of claim 22 (claim 36 depends upon claim 22). The word "the" before the recitation of "the pressure sensor" established antecedent basis back to claim 22.

Based on the above-amendment to the claims, the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Withdrawal of the rejection is respectfully requested.

**Issues Under 35 U.S.C. § 103(a) Obviousness**

The following prior art-based rejections are currently being maintained:

14. Claims 1, 5, and 11 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over **Huse *et al*** (U.S. 5,378,360), in view of **Bach *et al*** (U.S. 4,133,804), and **Kojima *et al*** (U.S. 6,179,569);
15. Claim 2 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over **Huse *et al*** (U.S. 5,378,360), in view of **Bach *et al*** (U.S. 4,133,804), and **Kojima *et al*** (U.S. 6,179,569), as applied to claims 1, 5, and 11 above, further in view of **Maroth** (U.S. 3,811,442); and
16. Claim 12 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over **Huse *et al*** (U.S. 5,378,360), in view of **Bach *et al*** (U.S. 4,133,804), and **Kojima *et al*** (U.S. 6,179,569), as applied to claims 1, 5, and 11 above.

Applicants respectfully traverse the rejections.

*The Present Invention*

The claimed invention is drawn to an apparatus for separating and purifying nucleic acids which comprises an apparatus or a combination of at least two or more apparatuses for separating and purifying nucleic acids, wherein each apparatus comprises a pressure sensor, and the pressure in the accommodation part of each apparatus for separating and purifying nucleic acids can be independently detected,

which comprises:

a cylindrical syringe having a leading end part in which a first opening part is formed, a base end part in which a second opening part is formed and an accommodation part between said first opening part and second opening part, the accommodation part being able to hold sample solution therein;

a solid phase-holding member comprising a column with a circular shape, connected to said leading end part, a flow hole being formed at the leading end side of the solid phase-holding member; and

a solid phase comprising an organic polymer having a hydroxyl group on the surface thereof is accommodated in said solid phase-holding member, located at the first opening part, the solid phase being able to adsorb and desorb nucleic acids in a sample solution;

a pressure difference-generating apparatus,

wherein the pressure sensor is capable of detecting the pressure in the accommodation part is connected to an operation part of the pressure difference-generating apparatus which extends out of the syringe; and

methods for using said apparatus.

Applicants respectfully submit that the cited references neither teach nor fairly suggest all of the limitations set forth above.

#### *Distinctions Over the Cited References*

##### **Huse *et al.* (U.S. 5,378,360)**

Huse *et al.* discloses an apparatus and methods for purifying and separating materials using gel chromatography based only on size. The media contained in the disclosed column do not contain organic polymers having hydroxyl groups. Additionally the teachings of Huse *et al.* do not disclose or suggest the concept of absorption and desorption as a method of separation and purification. Moreover, nowhere in the reference is the purification and separation of nucleic acids disclosed. Huse *et al.* merely discloses separation by chromatography, which is distinct and unrelated to the present invention.

##### **Bach *et al.* (U.S. 4,133,804)**

The shortcomings of Huse *et al.* are not complemented by the disclosure of Bach *et al.* since there is no teaching of the nucleic acid separation and purification by absorption and desorption. Bach *et al.* do disclose a high content of hydroxyl groups in polysaccharide chains, however the concept is drawn to protein purification based on size, not nucleic acid purification and separation by absorption. Therefore it appears to be a teaching of non-analogous art.

Nowhere does Bach *et al.* teach or suggest nucleic acid isolation or purification, or in particular absorption and desorption in a pressurized system. The Bach *et al.* disclosure is solely drawn to protein purification. When comparing protein vs. nucleic acids for purification, they have different structures, different pI values, and different sizes. Thus, their methods of purification are distinct.

Additionally, the teaching of Bach *et al.* discloses a high content of hydroxyl groups throughout the polysaccharide chains in a column. This appears to teach away from the claimed invention. In the present invention the hydroxyl groups are concentrated in the solid phase only. Therefore, the purified nucleic acids are concentrated and can be competed off the solid phase by desorption. The Bach *et al.* disclosure cannot enable this property, because the hydroxyl groups are throughout the column. By applying the teachings of this reference, the captured nucleic acids are not concentrated in one area and will reabsorb throughout the entire length of the column when competing with the desorption buffer.

Neither Huse *et al.* nor Bach *et al.* provide any teachings relevant to how nucleic acids would behave in a purification procedure when protein purification concepts based solely on size are applied.

Therefore, the additional cited art of Bach *et al.* is incapable of curing the above noted deficiencies of Huse *et al.*, and thus are incapable of rendering the instant invention as claimed obvious.

Even if these references are combined, one skilled in the art could not obtain from such a combination any motivation to arrive at the presently claimed pressurized apparatus and methods for nucleic acid purification.

**Kojima *et al.* (U.S. 6,179,569) & Maroth (U.S. 3,811,442)**

Kojima *et al.* and Maroth merely disclose a liquid infusion device comprising a pressure sensor. Neither of these references is drawn to a purification device, an apparatus comprising a high content of hydroxyl groups located in a small region or any methods of nucleic acid purification.

Therefore, the additional cited art of Kojima *et al.* and Maroth is incapable of curing the above-noted deficiencies of Huse *et al.* and/or Bach *et al.*, and thus are incapable of rendering the instant invention as claimed obvious.

Legal Standard for Determining Prima Facie Obviousness

M.P.E.P. § 2143 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). Second, the Examiner has to provide some rationale for determining obviousness, wherein M.P.E.P. § 2143 set forth some rationales that were set established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Here, the Examiner has not appropriately resolved the *Graham* factors, including ascertaining the differences between the prior art and the claims that are at issue, and the rationale in combining the cited references is improper.

The rationale should be made explicit, *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), and the Examiner must interpret the reference as a whole and cannot pick and choose only those selective portions of the reference which support the Examiner's position. *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention.").

As the M.P.E.P. directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. See MPEP § 2143.03. MPEP § 2143.03 recites examples of Basic Requirements of a *Prima Facie* Case of Obviousness and seven exemplary rationales.



Note that the list of rationales provided is not intended to be an all-inclusive list. Other rationales to support a conclusion of obviousness may be relied upon by Office personnel.

However, Applicants fully address these rationales below. According to Applicants analysis below, the Examiner has not met the basic requirements of a *prima facie* case of obviousness. More specifically, Applicants contend that:

(A) Combining prior art elements according to known methods cited do not yield predictable results for an apparatus for absorption and desorption as a method of separation and purification of nucleic acids wherein an organic polymer having a hydroxyl group on the surface thereof is accommodated in said solid phase-holding member, located at the first opening part;

(B) Simple substitution of one known apparatus for size separation by chromatography, does not yield predictable results in regards to an apparatus for absorption and desorption and a method of separation and purification;

(C) There is no known technique to improve an nucleic acid separation and isolation apparatus wherein one skilled in the art would use hydroxyl groups on the surface, accommodated in the solid phase-holding member, located only at the first opening part;

(D) Applying known techniques as taught by Bach *et al.*, Kojima *et al.* and Maroth, applied to the primary reference of Huse *et al.* do not yield predictable results for said apparatus for absorption and desorption and a method of separation and purification as claimed;

(E) The Examiner cannot support the conclusion of "obviousness" on the basis "obvious to try" – there are no predictable methods or models cited by the Examiner that establish a reasonable expectation of success for said methods considering that it was not known how an apparatus for absorption and desorption as a method of separation and purification under pressure and wherein a pressure sensor detects the pressure in the container that has reached a certain preset pressure would affect the purity;

(F) There is no reason or rationale cited by the Examiner that may prompt variations from the disclosure of Huse *et al.*, Bach *et al.* and Kojima *et al.* that would result in the claimed apparatus and methods of its use;

(G) There is no proper teaching, suggestion, motivation, and/or reasonable expectation of success that would yield predictable results in the prior art as cited by the Examiner that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed apparatus for separation and purification of nucleic acids and methods for its use.

Overall, as discussed above, Huse *et al.* fail to disclose the instantly claimed apparatus, and this feature has not properly been accounted for in the Office Action. The cited secondary references fail to cure the deficiencies of the primary reference. Accordingly, the present invention is not rendered obvious in view of the teachings and disclosures of the cited modification of Huse *et al.*, and/or the further combination of Bach *et al.* , Kojima *et al.* and Maroth. Any contentions of the USPTO to the contrary must be reconsidered in view of the above remarks. Withdrawal of the rejections is respectfully requested.

### **CONCLUSION**

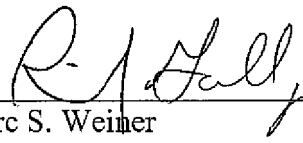
In view of the above amendments and Remarks, Applicants believe that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eggerton A. Campbell, Reg. No. 51,307, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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